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Research Article

Hematological Parameters in Beta Thalassemia Major Children

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Abstract
Background: Thalassemia is a hematological disorder that is caused by mutations in the genes that encode hemoglobin chains. Mutations in the β-globin gene are the most common cause of genetic disorders in humans. The objective of the study was to evaluate the hematological parameters in pediatric patients with beta thalassemia major. **Methods**: From January 2021 to November 2021, thirty beta thalassemia major children were recruited from the pediatric hematology outpatient clinic for this cross-sectional study at Minia University Children and Maternity Hospital. On the basis of their iron chelation therapy, the patients were divided into two groups: **Group I**: Deferasirox was administered to 15 patients as a single iron chelation therapy. **Group II**: Deferasirox and deferiprone were administered to 15 patients as part of combined iron chelation therapy; both drugs were given with one another every week for a period of 11 months. Furthermore, our patients were classified to splenectomized and unsplenectomized patients. All studied patients underwent a comprehensive clinical examination, history-taking, and laboratory investigations, including serum ferritin and complete blood count (CBC). **Results:** patients in group II required significantly more blood transfusions per year than those in group I, p= 0.007 and their disease duration was significantly longer, p < 0.0001. Hemoglobin, white blood cells and serum ferritin did not exhibit any substantial disparities between the studied groups. Splenectomized patients had higher platelet count compared to unsplenectomized counterparts, P= 0.047. **Conclusions:** Hematological parameters showed no significant differences among the studied groups of beta thalassemia major patients except for significantly higher platelet count in splenectomized patients. The combined treatment with deferasirox and deferiprone in a sequential manner doesn't seem to offer any more advantage compared to single therapy by deferasirox in decreasing serum ferritin between group I and group II. Antiplatelet treatment is essential for our splenectomized patients.

Keywords; Beta Thalassemia major; children; hematological parameters; deferasirox; deferiprone.

Introduction
Of all the hereditary conditions caused by decreased or absent hemoglobin chain synthesis, thalassemia is the most prevalent. An estimated 270 million people worldwide are thought to be carriers of various hemoglobinopathies, with 30% of them having β-thalassemia[(1).] Beta thalassemia major children develop iron overload after becoming transfusion dependent. Because of this, they are especially susceptible to iron excess in a number of organs, which can result in organ dysfunction. The primary goal of treatment continues to be effective iron chelation therapy [(2).] Three iron chelators are now accessible for clinical usage. Desferrioxamine administered parenterally, deferiprone, and deferasirox administered orally. Combination therapy denotes various strategies employed to attain negative iron balance when monotherapy is insufficient. It is possible to administer two iron chelators at the same time or on different days/weeks. [(3).]

Patients and methods
Thirty children with beta thalassemia major were involved in this cross-sectional study. Patients were collected as part of their

routine follow up at Minia University Children and Maternity Hospital's pediatric hematology outpatient clinic.

The patients were categorized into two groups: Group I: Fifteen patients received single iron chelation therapy (deferasirox). Group II: Fifteen patients received combined iron chelation therapy (deferasirox and deferiprone). Deferasirox was given orally once daily; Jadenu was given at a dose of 14 -28 mg/kg /day. Deferiprone was given orally at a dose of 75–100 mg/kg/day in 3 divided doses.

Both drugs were used in alteration way with one another every week for a period of 11 months. Blood samples were obtained prior to the transfusion. Parents were granted informed consent prior to enrollment. This study was also authorized by the Pediatric Department Council and the ethical committee of the Faculty of Medicine at Minia University. Afterward, all patients were evaluated through a review of their medical reports and subjected to the followings:

a. Careful history taking and clinical examination including: name, age, sex, amount of blood transfusion per year, duration of disease, and iron chelation therapy (type, dose, and duration), anthropometric measures as well as examination of chest, heart and abdomen.

b- Laboratory investigations:

CBC (it was performed using Celtac G, NIHON KIHODEN CORPORATION, automated hematology analyzer, JAPAN)

Serum ferritin: using autoanalyzer SELECTRA PROXL, ELITec. Group clinical chemistry automation system, Netherlands. Serum ferritin was measured every 3 months and mean value was calculated

Statistical analysis

Data analysis was done using IBM SPSS 26.0 (IBM; Armonk, New York, USA). Data normality was determined by Shapiro-Wilk or Kolmogorov-Smirnov tests. Quantitative data were reported as mean ± SD, with maximum and minimum ranges, and categorical data as count and percentage. Mann-Whitney test was used to compare non-parametric data between two independent groups, whereas independent t-test was used to compare numerical data. Chi-square or Fisher's exact tests compared categorical variables. A p-value below 0.05 was significant.

Results

The age in group I varied from 6 to 13.5 years, with a mean ± SD of 7.84 ± 2.38, while in group II, it ranged from 6 to 16 years, with a mean ± SD of 9.08 ± 2.5, P = 0.067. Group I had a male to female ratio of 4:11, while group II demonstrated a ratio of 9:6, p= 0.065. No significant differences were seen between the groups regarding age and sex. Group II needed significant higher amounts of blood transfusion/year with mean ± SD of 3615 ± 1773 with relatively smaller amounts in the group II with mean ± SD of 1920 ± 651.8, p= 0.007. Group II had significant longer duration of disease with mean ± SD of 11.6 ± 3.14 compared to group I of Mean ± SD 6.98 ± 2.2, p<0.0001. Three patients were splenectomized and 12 were unsplen-ectomized in group I, while 8 patients were splenectomized and 7 were unsplen-ectomized in group II, p= 0.058) **(Table 1)**.

Mean values of hemoglobin were 7.14 ± 0.8, 7.32±0.68 in group I and group II respectively. Mean values of white blood cells were 11.52 ±5.45, 11.98 ±4.96 in group I and group II respectively. Platelet count in group I had mean ± SD of 352.600 ±111.913, while group II had mean ± SD of 404.26 ±139.58. Serum ferritin had mean values of 2006.2± 740.76, 2180.26 ± 694.5 in group I and group II respectively. No significant differences were found regarding hemoglobin, white blood cells, platelet count or serum ferritin between the two groups, p=0.467, 0.693, 0.253, and 0.493 respectively **(Table 2)**.

On classifying our patients into splenic-tomized and unsplenectomized patients, 11patients were splenectomized and 19 were unsplenectomized. Splenectomized patients had higher platelet counts compared to unsplene-ctomized ones, P= 0.047. There were no significant differences regarding hemoglobin, white

blood cells, and serum ferritin between splenectomized and unspl-enectomized patients, P=0.812, P= 0.846, P= 0.747 respectively **(Table3)**

Table 1: Comparison of demographic and clinical data between group I and group II.

	Group I (N = 15)		Group II (N=15)		P value
	Mean ± SD	Range	Mean ± SD	Range	
Age (year)	7.84 ± 2.38	6 -13.5	9.08 ± 2.5	6-16	**0.067**
Sex: Male N (%) **Female N (%)**	4 (26.3%) 11 (73.3%)		9 (60%) 6 (40%)		**0.065**
Amount of blood transfusion (ml /kg /year)	1920 ± 651.8	1020 - 3000	3615.3 ± 1773.86	1260 - 7300	**0.007****
Duration of disease (year)	6.98 ± 2.2	6 – 12	11.6 ± 3.14	6.5 – 15.6	**<0.0001****
Splenectomy **Yes N (%)** **No N (%)**	3 (20%) 12 (80%)		8 (53.3%) 7 (46.7%)		**0.058**

*** Significant difference at P value < 0.05**

Table 2: Comparison between group I and group II regarding laboratory data

parameters	Group I (N = 15)		Group II (N=15)		P value
	Mean ± SD	Range	Mean ± SD	Range	
Hb (g/ dl)	7.14 ± 0.8	6 - 8.7	7.32 ± 0.68	6.3 - 8.7	**0.467**
WBCs (×10^3 /cmm)	11.52 ±5.45	4.6 – 25.3	11.98 ±4.96	6.7 -22	**0.693**
Platelets (×103/cmm)	352.600 ±111.913	284 - 625	404.26 ±139.58	200 -625	**0.253**
Ferritin (ng/ml)	2006.2 ± 740.76	1200-3350	2180.26 ± 694.5	1267 - 3415	**0.493**

Hb: hemoglobin; WBCs: white blood cells

Table 3: Comparison between splenectomized and unsplenectomized patients regarding laboratory data

parameters	Splenectomized patients (N = 11)		unsplenectomized patients (N = 19)		P value
	Mean ± SD	Range	Mean±SD	Range	
Hb (g/ dl)	7.23±0.847	6 -8.7	7.21±0.54	6.5 -8.1	**0.812**
WBCs (×10^3 /cmm)	12.3±6.43	6.7 -25.3	11.4±4.36	4.6 -19.2	**0.846**
platelets (×10^3/cmm)	453±149	208 - 625	335±90.5	184 -515	**0.047***
Ferritin (ng /ml)	2065±772	1267-3415	2109±694	1200-3350	**0.747**

Hb: hemoglobin; WBCs: white blood cells
***Significant difference at P value < 0.05**

Discussion

The variation in hematological parameters among beta thalassemia major children is illustrated in this study. We found that patients in group I required significantly more blood transfusions than those in group I. This is because group II has a prolonged clinical course than group I.

Regarding serum ferritin levels, no notable disparity was seen between group I and group II and the combination of defera-sirox and deferiprone did not provide any extra advantages regarding a substantial reduction in serum ferritin as compared to monotherapy with deferasirox. This is probably attributable to the consecutive not daily delivery of both medications of iron chelation. This is consistent with a study conducted by Prabhjot Jhinger et al., 2018 which determined that sequential combi-nation therapy was not superior to either drug alone[4]. In the other comparative studies by Totadri et al., 2015 and Gomber et al., 2016; serum ferritin in the combination group experienced a more significant decline[5,6]. In both studies,

doses of iron chelators were the same as we used in our study but administered as part of a daily regimen not in a sequential manner. Splenectomized group had greater platelet counts than their unsplenect-omized counterparts. This often seems to stem from chronic anemia, hyperplastic bone marrow, and the lack of platelet destruction by the spleen[7].

Consequently, in order to prevent thromboembolic complications, antiplay-telet therapy is required for our splenectomized patients. Furthermore, splenectomized patients showed no differ-ence in serum ferritin levels compared to unsplenectomized counter-parts; this can be explained by the fact that patients in our study were on combined chelation therapy following splenectomy. This is consistent with a study conducted by Belhoul et al., 2012 who found that serum ferritin in splenectomized patients were comparable to unsplenectomized ones[8].

But not in agreement with Aydinok et al., 2011 who stated that iron overload was significantly increased in splenectomized patients compared to unsplenectomized patients [9].

Conclusions

Hematological parameters showed no significant differences among the studied groups of beta thalassemia major patients except for significantly higher platelet count in splenectomized patients. The combined treatment with deferasirox and deferiprone in a sequential manner doesn't seem to offer any more advantage compared to single therapy by deferasirox in decreasing serum ferritin. Daily simulta-neous regimens of iron chelators could be used in place of sequential use every other week.

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